Mortality Rates Among Augmentation Mammoplasty Patients

An Update

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Background: A large follow-up study of cosmetic breast implant patients previously suggested an overall decrease in mortality but increased risks of brain and respiratory cancers and of suicides.

Methods: This cohort of 12,144 implant patients and 3614 patients with other types of plastic surgeries was followed for 5 additional years, enabling derivations of standardized mortality ratios (SMRs) based on population rates and relative risks (RRs) based on comparisons with the other patients.

Results: A total of 443 implant and 221 other plastic surgery patients were identified as deceased (SMR = 0.65 [95% confidence interval (CI) = 0.6–0.7] and 0.56 [0.5–0.6], respectively). Despite evidence that implants can interfere with mammographic visualization, there was no evidence that implant patients had a higher risk of death from breast cancer as compared with either the general population or other plastic surgery patients. The previous excess risk of brain cancer deaths among implant patients was attenuated by follow-up (as the result of no additional deaths; SMR = 1.43, 0.8–2.5; RR = 2.07, 0.5–8.9). A previously observed excess risk of respiratory cancer deaths persisted in comparisons with other plastic surgery patients (RR = 1.63; 1.0–2.7), but there was no evidence of a trend of risk with follow-up time. Implant patients also showed an elevated risk of suicide (SMR = 1.63, 1.1–2.3; RR = 2.58, 0.9–7.8) and of deaths caused by motor vehicle accidents (RR = 1.73; 0.6–5.4).

Conclusions: Although several elevations in cause-specific mortality were attenuated by additional follow-up, the excess risk of suicide among the implant patients remains of concern.

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Despite numerous investigations on the topic, the long-term health effects associated with breast implants remain uncertain. Whether breast implant patients experience unusual risks of mortality is an issue that has received limited attention. Mortality from breast cancer is of particular concern, given evidence that implants can interfere with the mammographic visualization of lesions.[1–5] There has been some evidence of a later presentation of disease among women with implants,[5–7] although this evidence has not been found in all studies.[8–11] In a previous evaluation of this issue among a large cohort of women, we found no evidence of an increase in breast cancer mortality rate among implant patients when compared with either the general population or an internal comparison series of women with other types of plastic surgery.[12] However, there was some evidence of increasing risks with follow-up time.[6] In addition, our study found substantial excess risks of brain cancers and suicides when breast implant patients were compared with the general population and an excess risk of respiratory cancers when compared with women seeking other types of plastic surgeries.[12] Subsequent studies have confirmed the elevated risk of suicide among breast implant patients[13–16] but have not provided confirmation of elevated risks of any cancers. However, most sites have been difficult to assess given small numbers of events.

To further assess mortality among patients with breast implants, we extended follow-up of our original cohort, adding 5 years of additional mortality data and nearly doubling the number of observed deaths. These data provided opportunities for assessing less common causes of death (including brain cancer) as well as for evaluating how mortality risks are affected by follow-up time.

METHODS

As detailed elsewhere,[6] this retrospective cohort study identified patients from 18 plastic surgery practices in 6 geographic areas (Atlanta, GA; Birmingham, AL; Charlotte, NC; Miami and Orlando, FL; and Washington, DC). We chose these practices because they had performed large numbers of cosmetic breast implant surgeries on a long-standing basis and were willing to give us unrestricted access to their records for purposes of subject identification and medical record abstraction. The National Cancer Institute's Institutional Review Board approved the study protocol and approach to patients, which included informed signed consent to seek details regarding health status and additional risk factor information.

The study focused on female subjects who had a first bilateral augmentation mammoplasty at these practices during the period of 1960–1988. Because studying breast cancer incidence was a primary goal of the study, patients receiving

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a breast implant after a diagnosis of breast cancer were not included. A total of 13,488 subjects were identified for study. In addition, attempts were made, after identification of approximately every third- to fourth-eligible breast implant patient, to identify a comparison patient who had another type of plastic surgery (not involving silicone) during the same time period and who were generally in the same age range as the breast implant patients. Comparison subjects were selected in all but one practice, where permission for access to records of such patients was denied. We identified a total of 3936 comparison subjects. Some patients had more than one operation but, when we prioritized them according to the following order of operations, 21% had abdominoplasties or liposuction; 34% blepharoplasties of rhytidectomies (operations for removal of wrinkles of the face or neck); 28% rhinoplasties, otoplasties, menoplasties or genioplasties (operations involving the nose, ear or chin); and 17% other types of plastic surgeries.

Trained medical record abstractors reviewed medical charts for eligibility. Using standardized software, data were directly entered into laptop computers. This information included patient identifiers as well as details on the types of surgery obtained (including implant type), any noted complications, and other factors that might affect health status (eg, weight).

In the initial morbidity follow-up of our cohort,[6] we had used a variety of sources (including telephone directories, credit bureaus, postmasters, and Motor Vehicle Administration records) to trace patients to allow direct contact for administration of questionnaires. We were unable to locate 20% of the cohort and had concentrated our previous mortality analyses[12] on located patients. Through the end of 1997, we had identified through the National Death Index (NDI) database a total of 258 implant patients and 128 control patients as deceased 1 or more years after the date of their initial plastic surgery. During the most recent mortality search, which covered the years 1998–2002, we submitted names of the remaining cohort members to the NDI and, among the previously nonlocated subjects, identified a sizeable number of deaths, particularly among the subjects for whom we had a core set of identifiers (name, date of birth, social security number), who comprised 52% of the nonlocated patients. We therefore focused current analyses on subjects who were likely to have been identified as deceased through linkage with the NDI, including previously located patients as well as nonlocated patients with identifiers. For these subjects, we accrued person-years beginning 1 year after the date of initial plastic surgery and continuing up until the time of death or for subjects not identified as deceased through the end of 2002. Previously nonlocated subjects without identifiers were not included in the accumulation of person-years. Among the included study subjects, we identified 185 additional deaths among the implant patients and 93 among the other plastic surgery patients, resulting in a total of 443 and 221 deaths, respectively. Codes for underlying causes of death were based on the International Classification of Diseases (9th revision) system, as available through the NDI-Plus database, or retrieved death certificates that were coded by trained nosologists.

Statistical Methods

We calculated mortality rates, standardized to the 1970 U.S. population, for both implant and other plastic surgery subjects. In addition, we computed standardized mortality ratios (SMRs) as the number of observed deaths divided by the expected number of events, based on age, race, and calendar year-specific mortality rates for females from U.S. mortality data available for the period 1970–2002.

We also conducted internal analyses, based on the relative risk (RR), of mortality in the breast implant patients compared with that of the other plastic surgery patients. We used Poisson regression methods, as implemented in the AMFIT module in the Epicure analysis package,[17] to calculate RRs, compute 95% confidence intervals (CIs), and adjust for potential confounding variables. For all analyses, the RR of implant status was adjusted for age at risk (5-year intervals through age 85), race (white or black), and calendar year of follow-up (1960–1964, . . ., 1995–1999, and 2000–2002).

RESULTS

The average age at entry into the cohort was 34 years among the implant patients compared with 41 years among the other plastic surgery patients. This age discrepancy reflects the fact that many of the other types of plastic surgeries, notably abdominoplasties, occurred at older ages than breast implants. The average time of cohort entry was more comparable between the 2 groups: late 1982 for the implant patients versus early 1984 for the other plastic surgery patients. The average years of follow-up for the 2 groups were 20.5 and 18.9 years, respectively.

The SMR for all causes of mortality was 0.65 (95% CI = 0.6–0.7) for the implant patients and 0.56 (0.5–0.6) for the other plastic surgery patients (Table 1). Among the implant patients, substantially decreased SMRs compared with the general population were observed for all malignancies, infectious and parasitic diseases, allergic, metabolic and nutritional diseases, diabetes, and diseases of the circulatory system. Similar decreases for these conditions were noted for the other plastic surgery patients. In contrast, a modest increase in the SMR among implant patients was found for suicides (1.63; 1.1–2.3), a relationship not observed among the other plastic surgery subjects.

The lower SMR from malignancies among the implant patients was reflected in the lower risk of breast (0.49; 0.3–0.7) and hematopoietic malignancies (0.44; 0.2–0.8), trends that were also observed among the other plastic surgery patients. In contrast to previous speculations that breast implants might increase the risk of multiple myeloma,[18] we observed no excess risk among the implant patients, with one death each in the implant and comparison groups. Although brain cancer previously showed a SMR of 2.45 (1.4–4.2), the absence of any additional deaths from this cause during the 5 additional years of follow-up resulted in an attenuation of the associated ratio (1.43; 0.8–2.5). Of interest, however, was an increased SMR of benign neoplasms among the implant

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TABLE 1. Age-Standardized Death Rates (Per 100,000 Person-Years [PYs]) and SMRs (Based on U.S. Mortality Rates, 1970–2002) Among Breast Implant and Other Plastic Surgery Patients, and Internally Derived RRs of Mortality for Implant versus Other Plastic Surgery Patients

	Implant Patients (PYs = 238,386)			Other Plastic Surgery Patients (PYs = 65,771)			Internal Comparison
	No. Deaths*	Rate†	SMR‡ (95% CI)	No. Deaths*	Rate†	SMR‡ (95% CI)	RR‡ (95% CI)
All causes of death	443	2.66	0.65 (0.6–0.7)	221	2.83	0.56 (0.5–0.6)	1.24 (1.0–1.5)
Infectious, parasitic diseases	10	0.07	0.63 (0.3–1.2)	2	0.03	0.28 (0.1–1.1)	2.68 (0.5–14.2)
All malignancies	184	1.08	0.66 (0.6–0.8)	94	0.99	0.63 (0.5–0.8)	1.22 (0.9–1.6)
Large intestine	11	0.03	0.62 (0.3–1.1)	12	0.09	1.07 (0.6–1.9)	0.60 (0.2–1.6)
Pancreas	6	0.04	0.57 (0.3–1.3)	4	0.08	0.58 (0.2–1.6)	1.50 (0.4–6.1)
Respiratory	54	0.57	0.83 (0.6–1.1)	26	0.31	0.65 (0.4–1.0)	1.63 (1.0–2.7)
Breast	33	0.08	0.49 (0.3–0.7)	12	0.10	0.40 (0.2–0.7)	0.98 (0.5–2.1)
Ovarian	14	0.09	0.75 (0.4–1.3)	8	0.07	0.82 (0.4–1.6)	1.34 (0.5–3.6)
Brain	13	0.03	1.43 (0.8–2.5)	3	0.03	0.74 (0.2–2.3)	2.07 (0.5–8.9)
Hematopoietic	10	0.03	0.44 (0.2–0.8)	6	0.07	0.47 (0.2–1.1)	1.14 (0.4–3.6)
Benign neoplasms	5	0.01	1.61 (0.7–3.9)	1	0.01	0.61 (0.1–4.3)	2.34 (0.2–23.7)
Allergic, metabolic, nutritional disorders	6	0.10	0.22 (0.1–0.5)	8	0.11	0.50 (0.2–1.0)	0.71 (0.2–2.3)
Mental disorders	6	0.02	1.02 (0.5–2.3)	3	0.04	0.92 (0.3–2.8)	0.91 (0.2–4.7)
Nervous system, sensory organ diseases	11	0.36	0.71 (0.4–1.3)	4	0.05	0.43 (0.2–1.2)	2.85 (0.7–10.9)
Diabetes mellitus	3	0.03	0.15 (0.0–0.5)	5	0.04	0.39 (0.2–0.9)	0.44 (0.1–2.0)
Circulatory system diseases	63	0.39	0.39 (0.3–0.5)	49	0.96	0.41 (0.3–0.5)	0.97 (0.6–1.5)
Arteriosclerosis, CHD	28	0.19	0.34 (0.2–0.5)	22	0.57	0.33 (0.2–0.5)	1.13 (0.6–2.1)
Vascular lesions	13	0.08	0.43 (0.3–0.7)	10	0.19	0.48 (0.3–0.9)	0.93 (0.4–2.4)
Respiratory diseases	37	0.24	0.82 (0.6–1.1)	21	0.19	0.62 (0.4–0.9)	1.73 (1.0–3.1)
Pneumonia	15	0.07	1.36 (0.8–2.3)	9	0.09	1.17 (0.6–2.2)	1.70 (0.7–4.2)
Digestive system diseases	20	0.06	0.63 (0.4–1.0)	9	0.07	0.55 (0.3–1.1)	1.08 (0.4–2.6)
Cirrhosis of liver	7	0.02	0.43 (0.2–0.9)	5	0.04	0.71 (0.3–1.7)	0.67 (0.2–2.5)
Senility, ill-defined diseases	5	0.10	0.60 (0.2–1.4)	4	0.08	1.16 (0.4–3.1)	0.88 (0.2–4.1)
All external causes	85	0.18	1.29 (1.0–1.6)	20	0.15	1.02 (0.7–1.6)	1.35 (0.8–2.3)
Accidents	44	0.11	1.15 (0.9–1.5)	14	0.11	1.12 (0.7–1.9)	1.05 (0.5–2.0)
Motor vehicle accidents	22	0.06	1.00 (0.7–1.5)	4	0.03	0.62 (0.2–1.6)	1.73 (0.6–5.4)
Suicides	29	0.06	1.63 (1.1–2.3)	4	0.03	0.85 (0.3–2.3)	2.58 (0.9–7.8)

*Shown are causes with at least 5 or more deaths in either the implant or other plastic surgery patients. Additional causes of death included the following (numbers in implant vs. other plastic surgery patients shown in parentheses): buccal cavity cancer (2, 2), esophageal cancer (1, 0), stomach cancer (2, 3), rectal cancer (3, 1), liver cancer (2, 1), larynx cancer (2, 0), cervical cancer (3, 3), uterine cancer (0, 2), bladder cancer (2, 2), kidney cancer (2, 4), thyroid cancer (0, 2), blood diseases (1, 0), rheumatic heart disease (2, 4), emphysema (3, 1), gastrointestinal ulcers (1, 0), genitourinary diseases (4, 4), skin and cellular tissue disease (1, 1), and bone diseases (2, 1).

†Age-standardized to the 1970 U.S. population.

‡SMRs and RRs adjusted for age, race, and calendar year.

patients (1.61; 0.7–3.9), with 4 of the 5 of these being of an unspecified nature in the brain and the fifth a benign neoplasm of the cerebral meninges.

Analyses based on internal comparison of the implant and other plastic surgery patients showed a slightly increased risk for all causes of death among the implant patients (RR = 1.24; 1.0–1.5). An elevation in risk was observed for all malignancies (1.22; 0.9–1.6), with this primarily reflecting higher rates of death from respiratory cancers among the implant patients (1.63; 1.0–2.7). Increased RRs also were observed for pancreatic (1.50; 0.4–6.1) and brain (2.07; 0.5–8.9) cancers, although based, respectively, on 6 and 13 deaths among the implant patients. The RRs for most other cancer sites, including breast cancer, were close to unity. For other causes of death, the major difference in risk between the 2 groups (as reflected through the internal comparison) was for motor vehicle accidents and suicides (1.73 [0.6–5.4] and 2.58 [0.9–7.8], respectively). Deaths resulting from infectious diseases, benign neoplasms, and nervous system disorders also were more common among the implant than the other plastic surgery patients, although with wide confidence intervals. No single infectious disease predominated among the implant patients, with septicemia and viral hepatitis being the most common causes of death. The elevated risk of nervous system disorders primarily reflected an excess of deaths caused by alcohol or drug dependence among the implant patients (5 deaths).

Table 2 presents SMRs among the implant patients by calendar year of implantation, age at initial breast implantation, and interval since implantation. For all causes of death,

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TABLE 2. SMRs for Selected Causes of Death Among Breast Implant Patients: Comparisons Based on U.S. Mortality Rates, 1970–2002

	All Causes		Malignancies		Circulatory System Diseases		Suicides	
	No. Deaths†	SMR*	No. Deaths†	SMR*	No. Deaths†	SMR*	No. Deaths†	SMR*
Calendar year at surgery								
<1975	69	0.63	27	0.60	12	0.42	3	1.30
1975–1979	195	0.77	89	0.85	26	0.41	9	1.53
1980–1984	120	0.57	50	0.58	16	0.33	10	1.71
1985+	59	0.55	18	0.42	9	0.41	7	1.86
Age at surgery (years)								
<35	162	0.65	58	0.60	17	0.37	16	1.41
35–39	84	0.60	40	0.64	14	0.44	4	1.15
40–44	78	0.68	37	0.73	10	0.34	6	3.42
45+	119	0.68	49	0.72	22	0.40	3	2.43
Interval since surgery (years)								
<10	78	0.47	31	0.48	8	0.24	8	0.96
10–14	105	0.67	42	0.64	12	0.34	10	2.27
15–19	121	0.71	62	0.86	15	0.35	8	2.56
20+	139	0.75	49	0.65	28	0.54	4	1.53

*SMRs adjusted for age, race, and calendar year.
†No. of deaths among implant patients.

there was a slight trend of increasing ratios with follow-up time (although all ratios remained less than unity), mainly reflecting the influence of deaths caused by circulatory diseases and suicides. There was little evidence that the ratio of deaths caused by malignancies increased with follow-up time. Of note was that those who were followed for 20 or more years continued to have a substantially lower ratio of death resulting from circulatory system diseases than the general population. The highest SMR for suicides was observed among women who received their implants at 40 years of age or older. The risk of death as the result of suicide was not elevated in the first 10 years of follow-up but was increased in all subsequent time periods.

When these same temporal relationships were assessed by comparing implant patients with the other plastic surgery patients (Table 3), somewhat higher risks of death were found for subjects who received their implants in the earlier calendar years. There was no evidence of a trend in risk with years of follow-up. Similar relationships according to calendar year were observed for deaths caused by malignancies. Little variation was found in the risks of death resulting from circulatory system disorders by these time parameters. The largest risk among implant patients was observed among those with 15–19 years of follow-up, albeit based on only 4 deaths. Deaths from suicide were difficult to interpret given the small numbers among the comparison patients, but there was no evidence for an increase in risk with follow-up time. Of note, however, was that the deaths caused by motor vehicle accidents among implant patients predominated in the later years, with 10 deaths occurring after 15 or more years of follow-up versus none among the other plastic surgery patients (data not shown).

When specific attention was focused on time trends for the 3 cancers of greatest interest (respiratory, breast, and brain) among the breast implant versus the other plastic surgery patients (Table 4), there was some evidence that the RRs of death from respiratory cancer decreased with follow-up time. Although there was somewhat of a trend of increasing SMRs with follow-up time for breast cancer among the implant patients, this pattern was not reflected in the RRs. Of note was that the RR associated with 20 or more years of follow-up was less than one (0.72). No additional brain cancers were observed during the latest follow-up period.

A total of 50% of the implant patients received silicone gel implants, 34% double-lumen implants, 12% saline-filled implants, 0.1% other types of implants, and 4% unspecified types of implants. The SMRs among breast implant patients for all causes of death did not vary substantially by the type of implants: 0.67 for silicone gel implants, 0.61 for double lumen implants, 0.67 for saline-filled implants, and 0.64 for unspecified types of implants. When individual causes of death were examined, there were, for the most part, no unusual relationships observed according to type of implant. The 2 possible exceptions were higher ratios among patients with double lumen implants for deaths caused by benign neoplasms (SMR = 3.52; 1.1–10.9) and suicide (2.25; 1.3–4.0), although both SMRs were based on fairly small numbers of deaths (3 and 12, respectively).

To determine the completeness of our efforts to identify deaths among all study subjects, we used alternative approaches to accumulating person-years. If we limited the analysis only to subjects that were located in our previous contact efforts, we

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TABLE 3. RRs for Selected Causes of Death Among Breast Implant Patients: Comparisons Based on Other Plastic Surgery Patients

	All Causes		Malignancies		Circulatory System Diseases		Suicides	
	No. Deaths†	RR*	No. Deaths†	RR*	No. Deaths†	RR*	No. Deaths†	RR*
Calendar year at surgery								
<1975	27	1.53	11	1.49	8	1.02	0	Infinity
1975–1979	66	1.36	28	1.28	15	1.02	0	Infinity
1980–1984	79	1.06	28	1.41	22	0.67	2	1.74
1985+	49	0.92	27	0.64	4	2.43	2	1.42
Age at surgery (years)								
<35	17	1.27	8	0.83	2	1.14	1	2.49
35–39	13	1.13	5	1.45	1	2.25	1	0.72
40–44	22	1.35	8	1.75	3	1.15	0	Infinity
45+	169	1.19	73	1.14	43	0.84	2	1.93
Interval since surgery (years)								
<10	51	1.00	24	0.91	7	1.29	0	Infinity
10–14	57	1.18	20	1.27	18	0.58	3	0.98
15–19	50	1.47	28	1.36	4	4.11	1	2.51
20+	63	1.08	22	1.00	20	0.74	0	Infinity

*RRs adjusted for age, race, and calendar year.
†Numbers of deaths among other plastic surgery patients. For numbers of deaths among implant patients, see Table 2.

accumulated 210,994 person-years among the implant patients and 58,097 among the other plastic surgery patients, and derived SMRs for all causes of death of 0.67 and 0.59, respectively. If we assumed complete identification of deaths by accumulating person-years for all subjects until the end of follow-up, we accumulated 272,239 person-years among the implant patients and 73,436 among other plastic surgery patients, with slightly lower associated SMRs (0.58 vs. 0.52). However, under either assumption, the RRs comparing the implant to the other plastic surgery patients were nearly identical to the figure of 1.24 in our main analyses (1.22 under the more-restrictive vs. 1.21 under the less-restrictive assumptions).

TABLE 4. SMRs Among Breast Implant Patients (Based on U.S. Mortality Rates) and RRs (Comparing Breast Implant Patients with Other Plastic Surgery Patients) for Deaths from Selected Cancers

	Respiratory Cancer			Breast Cancer			Brain Cancer		
	No. Patients Implant; Other Plastic Surgery	SMR*	RR*	No. Patients Implant; Other Plastic Surgery	SMR*	RR*	No. Patients Implant; Other Plastic Surgery	SMR*	RR*
Calendar year at surgery									
<1975	10; 1	0.90	9.52	6; 0	0.59	Infinity	0; 1	0.00	0.00
1975–1979	24; 8	0.95	1.77	15; 6	0.61	0.59	8; 0	2.46	Infinity
1980–1984	14; 11	0.70	1.24	8; 1	0.37	3.85	3; 2	1.03	1.89
1985+	6; 6	0.68	1.34	4; 5	0.36	0.60	2; 0	1.25	Infinity
Age at surgery (years)									
<35	11; 2	0.62	0.62	14; 3	0.51	0.47	5; 0	1.26	Infinity
35–39	10; 0	0.69	Infinity	8; 1	0.50	1.29	6; 0	3.00	Infinity
40–44	14; 3	1.04	1.84	6; 2	0.53	1.19	1; 0	0.69	Infinity
45+	19; 21	0.98	1.60	5; 6	0.40	1.19	1; 3	0.59	0.74
Interval since surgery (years)									
<10	7; 4	0.62	1.76	7; 4	0.37	1.07	4; 1	1.58	1.98
10–14	13; 4	0.89	2.24	7; 3	0.41	0.66	4; 1	1.79	2.10
15–19	15; 10	0.83	1.31	11; 2	0.67	1.23	5; 1	2.23	3.15
20+	19; 8	0.91	1.39	8; 3	0.55	0.72	0; 0	0.00	0.00

*SMRs and RRs adjusted for age, race, and calendar year.

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DISCUSSION

With 5 additional years of follow-up, this study provided enhanced opportunities to assess mortality associated with cosmetic breast implants. Women with breast implants and other types of plastic surgery were at a reduced risk of death from most causes as compared with the general population, supporting the notions that patients who choose to undergo plastic surgery are self-selected in terms of being healthy and that they may have greater interactions with the medical care systems in terms of screening and other preventive health measures. Of note was that even after 20 years of follow-up, both implant patients and those with other types of plastic surgery had substantially lower ratios of death as compared with the general population.

Given a lower ratio of deaths from all causes than the general population, the SMRs that were not reduced are noteworthy. For some causes of death, there were similar ratios observed for the implant and comparison patients, most likely reflecting that patients who seek various types of plastic surgery share certain lifestyle characteristics that are distinctive from other individuals.[19,20] Thus, the internal analyses that compared the mortality experience of implant patients to that of the other plastic surgery patients may be more informative in terms of determining the effects of implants on disease experience. However, given that the comparison series was only about one quarter of the size of the implant population (a reflection of the fact that the primary purpose of the study was to focus on cancer incidence, for which external incidence rates are available), some comparisons were limited by small numbers of events.

Despite the fact that this extended follow-up nearly doubled the number of events, most results were similar to those previously observed. There were particular strengths for evaluating long-term trends, because the average length of follow-up among implant patients was extended from approximately 14 to 19 years. These additional years of follow-up are increasingly important, given the relatively young age of the cohort members at entry (34 years among the implant and 41 among the other plastic surgery patients). The additional years translate into increased numbers of women entering ages when cancers become more common, and a corresponding increase in the number of expected events. Thus, this study had advantages for evaluating long-terms risks of breast, brain and respiratory cancers, for which previous analyses had raised some concerns.

The effect of breast implants on breast cancer mortality is of particular concern, given extensive evidence that implants interfere with mammographic and clinical evaluation of breast lesions. In addition, several studies have suggested that patients with breast implants present at somewhat-later stages of disease than other patients.[5–7] Studies that have attempted to evaluate breast cancer mortality among implant patients, however, have been limited by small numbers of events. Previous investigations, including our previous follow-up,[11–13] have shown decreases in risk when breast implant patients have been compared with women in the general population. Although these results would be expected for short follow-up periods, given that patients with historical or pre-existing breast cancers at the time of implantation (ie, prevalent cancers) would be excluded from breast implant cohorts,[6] questions remain as to long-term effects. However, our current results provide no support for increased mortality from breast cancer among breast implant patients, even after 20 years of follow-up.

Our previous observation of an elevated risk of brain cancer among implant patients was difficult to evaluate given small numbers and concerns regarding the accuracy of the diagnoses defined through death certificates. Although retrieval of pathology records for the majority of these deaths confirmed the origin of the cancer as being in the brain,[21] other studies have not observed an excess risk of brain cancers among implant patients; however, these other studies involved small numbers (1 in a Finnish study,[22] 3 each in U.S.[23] and Danish[24] studies, and 4 in a Swedish study[25]). Our latest follow-up did not identify any additional deaths caused by brain cancer, resulting in an attenuation in both the associated SMR (1.43) and RR (2.07) as compared with previous results. The current analyses did show a persistent increased SMR for benign neoplasms of the brain. However, even if all of these benign neoplasms were misdiagnosed and were truly brain cancers, the resultant SMRs would have been 1.48 (observed = 18, expected = 12.2) for the implant patients and 0.70 (observed = 4, expected = 5.7) for the comparison patients, and homogeneity of the 2 SMRs could not be rejected ($P = 0.17$).

In both our previous investigation, as well as in a Swedish study,[13] increased risks of death from respiratory cancers were observed among breast implant patients. The Swedish researchers attributed their finding to higher rates of smoking among implant patients, a characteristic that did not appear to explain the higher rate of respiratory cancer between implant and comparison patients in our study.[19] In the present follow-up the RR comparing implant to other plastic surgery patients for respiratory cancer was reduced to 1.63 (1.0–2.7). We saw no evidence of any relationship of risk with years of follow-up, suggesting that the association might not be causal.

A number of studies, including our previous follow-up effort as well as investigations in Sweden,[13] Finland,[16] and Denmark,[14] have all found higher rates of death from suicide than comparably aged women in the general population, with the existing literature showing 58 observed versus 25.2 expected deaths (overall SMR = 2.3, 1.7–3.0).[15] The present analysis contributed 10 additional deaths from suicide among implant patients, with the SMR being 1.63 when comparisons were made with the general population and the RR being 2.58 in comparison with other plastic surgery patients. The increase in risk was not apparent until 10 or more years after implantation, with no evidence of further increases for those with extended follow-up. This pattern of risk differs from results of studies in Denmark, where high ratios were observed in all time periods,[14] and in Finland, where the highest ratio was observed within the first 5 years after breast implantation, although based on only 6 deaths.[16]

Reasons for the excess risk of suicide among implant patients remain unclear, although predisposing personality

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characteristics have been suggested as a possible contributing factor. Women seeking breast implants have been shown to demonstrate varying degrees of low self esteem, anxiety, anddepression.[26–33] Postimplantation dissatisfaction might also be involved, especially given well-documented short-term complications associated with implants.[34] Some support for this latter possibility derives from studies in Denmark, which show that women seeking implants have similar frequencies of previous depression as other patients[35] but higher rates of postimplantation use of psychotropic drugs.[36] However, a recent study[14] found a higher prevalence of psychiatric admissions before cosmetic surgery among women undergoing breast implant surgeries than among women undergoing breast reduction or other cosmetic surgery procedures. These findings have led to the recommendation that women seeking breast implant surgery undergo psychologic evaluations, including appraisal of past psychiatric symptoms and disorders, to assure that they are suited for the procedure.[15]

A new finding that emerged from our study was an elevated risk of death from motor vehicle accidents when implant patients were compared with the other plastic surgery patients. Most of the excess occurred among patients with extended follow-up. This issue has not been assessed extensively in previous investigations, although one study in Sweden noted that breast implant patients experienced higher rates of deaths from unintentional injuries.[13] Given that we observed no excess risk for other types of accidents, this finding suggests that some of these vehicular deaths were not entirely accidental. Alternatively, some of these accidents may have been related to alcohol and drug exposures, given that we observed higher rates of deaths due to these dependencies among the implant patients.

In summary, during this extended follow-up, both breast implant and other plastic surgery patients continued to show lower rates of death than the general population. This was true even for breast cancer, most likely reflecting that implant and other plastic surgery patients have good access to medical care. In terms of risk of death from malignancies, most sites were not elevated among the breast implant patients. Previously observed increased risks related to brain and respiratory cancers were attenuated with additional follow-up and detailed analyses by follow-up time did not support a notion of causality. Suicides continued to be excessive among breast implant patients, with some suggestion that there might also be an increased risk associated with deaths caused by motor vehicle accidents.

REFERENCES

1. Carlson GW, Curley SA, Martin JE, Fornage BD, Ames FC. The detection of breast cancer after augmentation mammaplasty. *Plast Reconstr Surg*. 1993;91:837–840.
2. Eklund GW, Cardenosa G. The art of mammographic positioning. *Radiol Clin North Am*. 1992;30:21–53.
3. Fajardo LL, Harvey JA, McAleese KA, Roberts CC, Granstrom P. Breast cancer diagnosis in women with subglandular silicone gel-filled augmentation implants. *Radiology*. 1995;194:859–862.
4. Handel N, Silverstein MJ, Gamagami P, Jensen JA, Collins A. Factors affecting mammographic visualization of the breast after augmentation mammaplasty. *JAMA*. 1992;268:1913–1917.
5. Silverstein MJ, Handel N, Gamagami P, et al. Breast cancer diagnosis and prognosis in women following augmentation with silicone gel-filled prostheses. *Eur J Cancer*. 1992;28:635–640.
6. Brinton LA, Lubin JH, Burich MC, Colton T, Brown SL, Hoover RN. Breast cancer following augmentation mammoplasty (United States). *Cancer Causes Control*. 2000;11:819–827.
7. Skinner KA, Silberman H, Dougherty W, et al. Breast cancer after augmentation mammoplasty. *Ann Surg Oncol*. 2001;8:138–144.
8. Birdsell DC, Jenkins H, Berkel H. Breast cancer diagnosis and survival in women with and without breast implants. *Plast Reconstr Surg*. 1993;92:795–800.
9. Brinton LA, Malone KE, Coates RJ, et al. Breast enlargement and reduction: results from a breast cancer case-control study. *Plast Reconstr Surg*. 1996;97:269–275.
10. Clark CP III, Peters GN, O'Brien KM. Cancer in the augmented breast. Diagnosis and prognosis. *Cancer*. 1993;72:2170–2174.
11. Deapen D, Hamilton A, Bernstein L, Brody GS. Breast cancer stage at diagnosis and survival among patients with prior breast implants. *Plast Reconstr Surg*. 2000;105:535–540.
12. Brinton LA, Lubin JH, Burich MC, Colton T, Hoover RN. Mortality among augmentation mammoplasty patients. *Epidemiology*. 2001;12:321–326.
13. Koot VC, Peeters PH, Granath F, Grobbee DE, Nyren O. Total and cause specific mortality among Swedish women with cosmetic breast implants: prospective study. *BMJ*. 2003;326:527–528.
14. Jacobsen PH, Holmich LR, McLaughlin JK, et al. Mortality and suicide among Danish women with cosmetic breast implants. *Arch Intern Med*. 2004;164:2450–2455.
15. McLaughlin JK, Wise TN, Lipworth L. Increased risk of suicide among patients with breast implants: do the epidemiologic data support psychiatric consultation? *Psychosomatics*. 2004;45:277–280.
16. Pukkala E, Kulmala I, Hovi SL, et al. Causes of death among Finnish women with cosmetic breast implants, 1971–2001. *Ann Plast Surg*. 2003;51:339–342.
17. Preston DL, Lubin JH, Pierce DA, McConney ME. *Epicure User's Guide*. Seattle, WA: Hirosoft International Corporation; 2002.
18. Potter M, Morrison S, Wiener F, Zhang XK, Miller FW. Induction of plasmacytomas with silicone gel in genetically susceptible strains of mice. *J Natl Cancer Inst*. 1994;86:1058–1065.
19. Brinton LA, Brown SL, Colton T, Burich MC, Lubin J. Characteristics of a population of women with breast implants compared with women seeking other types of plastic surgery. *Plast Reconstr Surg*. 2000;105:919–927.
20. Fryzek JP, Weiderpass E, Signorello LB, et al. Characteristics of women with cosmetic breast augmentation surgery compared with breast reduction surgery patients and women in the general population of Sweden. *Ann Plast Surg*. 2000;45:349–356.
21. Brinton LA, Lubin JH, Burich MC, Colton T, Brown SL, Hoover RN. Cancer risk at sites other than the breast following augmentation mammoplasty. *Ann Epidemiol*. 2001;11:248–256.
22. Pukkala E, Boice JD Jr, Hovi SL, et al. Incidence of breast and other cancers among Finnish women with cosmetic breast implants, 1970–1999. *J Long Term Eff Med Implants*. 2002;12:271–279.
23. McLaughlin JK, Lipworth L. Brain cancer and cosmetic breast implants: a review of the epidemiologic evidence. *Ann Plast Surg*. 2004;52:115–117.
24. Mellemkjaer L, Kjoller K, Friis S, et al. Cancer occurrence after cosmetic breast implantation in Denmark. *Int J Cancer*. 2000;88:301–306.
25. McLaughlin JK, Nyren O, Blot WJ, et al. Cancer risk among women with cosmetic breast implants: a population-based cohort study in Sweden. *J Natl Cancer Inst*. 1998;90:156–158.
26. Baker JL Jr, Kolin IS, Bartlett ES. Psychosexual dynamics of patients undergoing mammary augmentation. *Plast Reconstr Surg*. 1974;53:652–659.
27. Beale S, Hambert G, Lisper HO, Ohlsen L, Palm B. Augmentation mammaplasty: the surgical and psychological effects of the operation and prediction of the result. *Ann Plast Surg*. 1984;13:279–297.
28. Meyer L, Ringberg A. Augmentation mammaplasty—psychiatric and psychosocial characteristics and outcome in a group of Swedish women. *Scand J Plast Reconstr Surg Hand Surg*. 1987;21:199–208.

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29. Ohlsen L, Ponten B, Hambert G. Augmentation mammaplasty: a surgical and psychiatric evaluation of the results. *Ann Plast Surg*. 1979;2: 42–52.
30. Shipley RH, O'Donnell JM, Bader KF. Personality characteristics of women seeking breast augmentation. *Plast Reconstr Surg*. 1977;60: 369–376.
31. Birtchnell S, Whitfield P, Lacey JH. Motivational factors in women requesting augmentation and reduction mammaplasty. *J Psychosom Res*. 1990;34:509–514.
32. Schlebusch L, Mahrt I. Long-term psychological sequelae of augmentation mammoplasty. *S Afr Med J*. 1993;83:267–271.
33. Sihm F, Jagd M, Pers M. Psychological assessment before and after augmentation mammaplasty. *Scand J Plast Reconstr Surg*. 1978;12: 295–298.
34. Gabriel SE, Woods JE, O'Fallon WM, Beard CM, Kurland LT, Melton LJ III. Complications leading to surgery after breast implantation. *N Engl J Med* 1997;336:677–682.
35. Kjoller K, Holmich LR, Fryzek JP, et al. Characteristics of women with cosmetic breast implants compared with women with other types of cosmetic surgery and population-based controls in Denmark. *Ann Plast Surg*. 2003;50:6–12.
36. Breiting VB, Holmich LR, Brandt B, et al. Long-term health status of Danish women with silicone breast implants. *Plast Reconstr Surg*. 2004;114:217–226.

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